Newborn screening in South Australia: is it universal?

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ABSTRACT

Objective: To determine the biochemical screening rate of newborns in South Australia and the factors associated with babies not being screened.

Design: Matching of data in the SA Newborn Screening Centre database (acquired from Guthrie cards) with the SA perinatal data collection (compiled from supplementary birth records) to determine how many newborns missed screening. Risk factors for missed screening were identified from sociodemographic and clinical variables recorded in the perinatal data collection and analysed by multivariable unconditional logistic regression analysis.

Patients and setting: All live births ($n = 18\,426$) in South Australia in 1999, in the 63 hospitals assisting deliveries or in the home.

Main outcome measures: Rates of biochemical screening and missed screening in all newborns and among various subgroups; adjusted odds ratios (after multivariable logistic regression analysis) for risk factors for missed screening.

Results: The newborn screening rate in South Australia in 1999 was 97.8%. Babies born at home, born to an Aboriginal mother, or born to a mother who normally resided in another state were at higher risk of missed screening. Other factors associated with missed screening were having fewer than seven antenatal visits, prematurity (gestational age at birth < 32 weeks), congenital abnormality in the baby, use of paediatric intensive care, early discharge from hospital before 3 days (but especially after less than 1 day), and death of the baby during the neonatal period.

Conclusion: In South Australia, while 2.2% of all newborns missed screening in 1999, in certain high-risk groups the proportions of unscreened babies were significantly higher. With a 2% missed screening rate, one might expect one newborn with a screening-detectable disorder to elude detection every other year in South Australia.

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WITH THE ADVENT of the Guthrie test for phenylketonuria in 1961, a new era in medicine began. Biochemical screening of newborns has become a well established public health measure in most developed countries.[1,2] The current newborn screen in South Australia can detect galactosaemia, congenital hypothyroidism, cystic fibrosis and up to 30 additional disorders, amino-acidopathies, organic-acidurias and fatty-acid oxidation defects by tandem mass spectrometry.[3-6] While each of these disorders is rare individually, in aggregate they are not. Biochemical screening of newborns now finds one true positive result (ie, one significant treatable disorder) for every 800 babies screened by the SA Newborn Screening Centre (NSC).

Data on the proportion of newborns who are screened in such programs are limited. A survey distributed to 40 laboratories in 35 countries of North and South America, Europe, Asia and Australasia determined a self-reported newborn screening rate of > 99% in 13 programs, 95%–98% in seven, < 95% in three, and no data for the remainder.[7] A large study in Alberta, Canada, in which live-birth registration data were matched with newborn screening data, reported a screening rate of 98%.[8] Objective Australian data are lacking.

We present here the results of an audit to determine the rate of newborn screening in South Australia and identify some of the factors associated with babies not being screened.

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METHODS

Sources of neonatal data

In South Australia, the hospital of birth is responsible for collecting and delivering a sample of each baby's blood to the SA NSC. Collection of the sample is typically done by neonatal nurses or midwives. At 2 days of age, a blood sample from each newborn is collected onto specially printed filter paper (the "Guthrie card"), which includes identifying data (Box 1).[9] Even in the event of neonatal death, it is recommended that a Guthrie card sample be taken (the sample is also used as part of the biochemical autopsy in postmortem examinations). If parents refuse consent, the NSC still requests that a card with identifying data but no blood be sent to the NSC.

Babies leaving hospital before 2 days of age are dealt with individually. If the midwife in attendance considers that the domiciliary service will be able to successfully collect a sample at two days, the baby is referred to the domiciliary service. If success is unlikely, a sample is collected before discharge as a back-up.

1: Sociodemographic variables recorded on supplementary birth records and Guthrie cards

Supplementary birth record	Guthrie card
Mother's surname(s) and initials	Mother's surname and given name
Mother's UR number	Mother's UR number
State of residence	
Postcode	
Statistical local area	
Local government area	
Mother's date of birth	Mother's date of birth
Race	
Country of birth	
Type of patient (public or private)	
Marital status	
Occupation	
Hospital/place of birth	Hospital/place of birth
Baby's UR number	Baby's UR number
Baby's surname	Baby's surname and given name
Baby's date and time of birth	Baby's date and time of birth
Baby's sex	Baby's sex
Baby's birth order (in multiple births)	Baby's birth order (in multiple births)

UR = unit record.

Guthrie cards are delivered to the NSC either by courier or by post. The identifying data from the cards (Box 1) are entered into the NSC database, and the cards are usually analysed within one day of receipt. Positive results are followed up by the NSC or, when indicated, by the Metabolic Unit of the Department of Chemical Pathology at the Women's and Children's Hospital. Negative reports are returned to the hospital of birth within 3 weeks as laboratory reports for inclusion in the newborn's case notes.

All births of at least 20 weeks' gestation or 400 g birthweight in South Australia are required by legislation to be notified to the Pregnancy Outcome Unit of the Epidemiology Branch, Department of Human Services. This is undertaken by hospital and homebirth midwives or neonatal nurses, who record data in a supplementary birth record (SBR) for each child. The SBR contains many sociodemographic and clinical variables used for monitoring pregnancy outcome (Box 1). (These data have been shown to be very reliable when compared with hospital case records.[10]) Combined data from SBRs make up the SA "perinatal data collection". Statistical summaries of these data are provided in the annual report of the Pregnancy Outcome Unit[11] and on the Department's website (www.dhs.sa.gov.au/pehs/pregnancy-outcome.htm).

Data matching

Using Automatch software,[12] we matched babies born in 1999, as recorded on SA NSC Guthrie cards, with live births recorded in the SA perinatal data collection. (Automatch is a probabilistic linkage technology used for linking large public health databases in a statistically justifiable manner, matching two files of individual data under conditions of uncertainty.[13]) The matching variables were mother's surname, baby's surname, dates of birth and hospital unit record numbers of mother and baby, baby's sex, and birth order (in multiple births). All matching and analyses on deidentified data were undertaken within the Epidemiology Branch.

A small number of births each year, mainly homebirths, are not notified to the Pregnancy Outcome Unit.[11] All these additional homebirths in 1999 were identified from the SA Births, Deaths and Marriages register. Babies with NSC Guthrie cards who could not be matched with the perinatal data collection were further matched with births identified in the SA Births, Deaths and Marriages register. (The Births, Deaths and Marriages register could not be used as the principal source of data for our study, as it does not contain the extensive sociodemographic and clinical data available in the perinatal data collection, and has less complete ascertainment of births, except homebirths, than the perinatal data collection.[14])

Statistical analysis

We first calculated univariate odds ratios (ORs) for sociodemographic and clinical factors from the perinatal data collection to determine their association with not having a Guthrie test. All potential candidate variables with $P \leq 0.15$ were then entered into a multivariable unconditional logistic regression analysis using Stata software.[15] Variables were tested for interactions and collinearity. All models were developed by backward elimination, retaining variables with $P < 0.05$ in the final models, which were tested for goodness of fit using the Hosmer–Lemeshow test.[15]

RESULTS

Of 18 318 Guthrie cards collected in 1999, 261 were repeat samples, leaving 18 057 individual births with cards; 17 997 of these cards were matched to Pregnancy Outcome Unit data (SBRs), leaving 60 cards unmatched. Of the 60 unmatched cards, 16 (eight homebirths, eight hospital births) could be matched to records in the Births, Deaths and Marriages data collection. The 44 cards that had no match with either of the above data collections are likely to represent babies who were born interstate and transferred to South Australia after birth.

Of the 18 404 live births notified to the Pregnancy Outcome Unit in 1999, 407 had no matching Guthrie card and thus had missed screening.

Twenty-two births (14 homebirths, eight hospital births) identified in the SA Births, Deaths and Marriages data collection were not notified to the Pregnancy Outcome Unit.

Overall, 413 newborns (407 recorded in the perinatal data collection and 6 additional in the Births, Deaths and Marriages data collection) out of a total of 18 426 live births (18 404 and 22 in the respective collections) were unmatched to Guthrie cards and considered unscreened. The missed Guthrie screening rate was therefore 2.2%.

Sociodemographic factors

There were no significant differences in newborn screening rate associated with sex of baby, maternal age, marital status, patient type (private or public), type of hospital (teaching, private or

2: Risk factors for missed biochemical screening of newborns

Factor	Missed screening rate	Adjusted odds ratio (95%CI) for missed screening
Race		
White*	2.2% (367/16953)	1.00
Aboriginal	5.4% (24/443)	1.94 (1.24–3.03)
State of usual residence		
South Australia	2.2% (399/18309)	1.00
Another state	12.0% (14/117)	4.44 (2.38–8.28)
Place of birth of baby†		
Hospital	2.2% (399/18374)	1.00
Home	26.9% (14/52)	18.57 (9.97–34.59)
Number of antenatal visits†		
⩾ 7	2.0% (290/14446)	1.00
< 7	4.4% (54/1236)	1.48 (1.05–2.09)
Plurality		
Singleton birth	2.3% (409/17863)	1.00
Multiple birth	1.0% (4/563)	0.33 (0.12–0.90)
Gestational age at birth		
⩾ 37 weeks	2.1% (359/16986)	1.00
< 32 weeks	8.7% (20/231)	3.23 (1.89–5.52)
Congenital abnormality		
Absent	2.1% (375/17980)	1.00
Present	7.5% (32/424)	2.67 (1.70–4.18)
Paediatric intensive care		
Not used	2.2% (399/18357)	1.00
Used	17.0% (8/47)	4.23 (1.76–10.16)
Baby's length of stay in hospital		
⩾ 3 days	1.8% (247/14046)	1.00
< 1 day	11.1% (34/307)	6.16 (4.16–9.13)
1 day	3.6% (45/1255)	2.17 (1.56–3.00)
2 days	2.6% (73/2761)	1.62 (1.24–2.12)
Neonatal death (in first 28 days)†		
Survivor	2.1% (386/18388)	1.00
Neonatal death	71.1% (27/38)	44.10 (19.78–98.34)

* Does not include Asian women and women from certain other ethnic minority groups.
† Evaluated in a separate model.

rural), size of hospital, metropolitan or rural residence in South Australia, or country of birth (born in Australia, another English-speaking country, or a non-English-speaking country).

However, babies who were born at home, born to Aboriginal mothers or born to mothers who usually lived in another state had significantly higher missed Guthrie screening rates. After multivariable logistic regression analysis, these remained independent risk factors for missed screening (Box 2). Homebirth as a risk factor was confirmed in a separate multivariable model that excluded length of stay in hospital, as this was not applicable to homebirths.

Clinical factors

Risk factors for missed Guthrie screening were having fewer than seven antenatal visits, prematurity (gestational age at birth < 32 weeks [but not 32–36 weeks]), congenital abnormality in the baby, use of paediatric intensive care, discharge from hospital after less than 3 days, and death of the baby during the neonatal period (ie, the first 28 days of life) (Box 2). There were no differences in screening rate with increasing parity, except for parity ⩾ 3. Multiple-birth babies were significantly less likely to miss screening than singletons.

After multivariable logistic regression analysis, all of these factors, except for parity ⩾ 3, remained independent risk factors for missed Guthrie screening, and multiple birth remained protective. While length of hospital stay was a significant risk factor for any baby discharged less than 3 days after birth, babies staying less than 1 day were at particular risk of missed screening.

Although having fewer than seven antenatal visits was an independent risk factor, this variable was evaluated in a separate model, as this information was missing from a large number of records (2744, or 14.9%). Neonatal death, also a strong risk factor, was evaluated separately, as it was considered to be less clinically relevant than other risk factors.

DISCUSSION

Our audit shows that newborn screening in South Australia is not universal. Although the overall missed screening rate in the population is about 2.2%, there are subgroups of newborns with missed screening rates in excess of 20%. A screening rate of 97.8% is comparable with that found in other studies.[7,8]

Our study had the advantage of being based on large and fairly comprehensive bodies of data, collected routinely from a relatively well circumscribed population. The Guthrie database is maintained by the SA NSC staff, who constantly review their database in day-to-day clinical use. Guidelines are provided to midwives for the perinatal data collection to improve uniformity in data provision, and there are many validation checks in place for the database. The routine collection of the data also reduces reporting bias. The matching and analysis were undertaken by staff familiar with Automatch and the intricacies of the perinatal data collection, and access was provided to the Births, Deaths and Marriages database for complete ascertainment of births.

On the other hand, in matching two large databases (each containing about

18 000 records), errors or missing data within each database may be compounded by errors in the matching process.

The screening rates for babies at greater risk of missed screening may be improved by directing additional attention to at-risk groups. Raising the awareness of hospital staff, especially those in paediatric intensive care or those caring for babies who are very premature or have congenital abnormalities, could help to increase the screening rate. Likewise, alerting homebirth midwives and nurses who visit early-discharged babies to the problem of missed screening could improve coverage. Aboriginal mothers, mothers from interstate and those who have had less antenatal care also need special attention from healthcare workers.

Although biochemical screening is recommended for babies who die in the neonatal period, including those who have an autopsy, screening has often not been performed, even though blood samples may have been taken for some other purpose. The SA NSC has asked to be advised of births for which there has been parental refusal for screening, but there is uncertainty about whether all of these are notified.

In Birmingham, UK, a system in which births are reported independently in real time to the regional newborn screening centre has operated for 15 years.[16] Birth reports are sent electronically via a closed-loop system to the newborn screening centre, where they are matched with Guthrie cards. In the event that no match can be found, the centre follows up the baby to ensure screening. This system has resulted in screening rates of 99.5%. The same method has been adopted in the London area over the past 5 years, with reported screening rates of 99.9%.[17] In South Australia, where 63 hospitals assist deliveries, a system like this would greatly help in making newborn screening truly universal.

Thus, there are many areas for improvement of the screening service. With around 18 000 children born each year in South Australia and 1 in 800 having a detectable disorder, a 2% missed screening rate means there is the potential to miss a child with a serious detectable disorder every other year.

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COMPETING INTERESTS

None identified.

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